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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/745,095	12/20/2000	Leah E. Appel	PC10818AJTJ	8852

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Gregg C. Benson
Pfizer Inc. MS 4159
Eastern Point Road
Groton, CT 06340

EXAMINER	
GOLLAMUDI, SHARMILA S	

ART UNIT	PAPER NUMBER
1616	20

DATE MAILED: 10/30/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/745,095	Applicant(s) APPEL ET AL.	
	Examiner Sharmila S. Gollamudi	Art Unit 1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 August 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *See Continuation Sheet* is/are pending in the application.

4a) Of the above claim(s) *58-62* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,7-9,12-32,44,45,49-51,56-81,88-97,101,103-108,118-122,124,130 and 131* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Continuation of Disposition of Claims: Claims pending in the application are 2,7-9,12-32,44,45,49-51,56-81,88-97,101,103-108,118-122,124,130 and 131.

DETAILED ACTION

Receipt of Request for Continued Examination, Extension of time, and Amendment C received on August 21, 2003 is acknowledged. Receipt of Supplementary Information Disclosure received on September 4, 2003 is acknowledged. Claims 2, 7-9, 12-32, 44-45, 49-51, 56-57, 63-81, 88-97,101, 103-108, 118-122, 124, and 130-131 are pending in this application.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 2, 7-9, 12-32, 44-45, 49-51, 56, 63-81, 88-97,101, 103-108, 118-122, 124, and 130-131 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wong et al (4,765,989) in view of Stevens et al (5,897,874).

Wong et al teach an osmotic device for administering drugs in various shapes and forms. The object of the device is to provide a therapeutic device that administers a

complete pharmaceutical regimen at a controlled and continuous time period. The device also provides dispending to the gastric tract at a controlled rate. See column 3. The device contains a first composition containing drug, polyethyleneoxide (PEO) (drug entertaining agent), hydroxypropylmethylcellulose (HPMC) (concentration enhancing polymer), and magnesium stearate (tabletting aid). The second expanding composition contains PEO (swelling agent), HPMC (concentration enhancing polymer), sodium chloride, and magnesium stearate (tabletting aid). The osmopolymers used in the invention have an expansion factor of 2-50 fold volume increase in the presence of aqueous or biological fluid (col. 16, lines 3-5). The mass ratio of the first composition to the second composition is taught on column 16. The swelling ratio is taught on columns 17 and 18. Wong teaches the active agent may in various forms and dispersed in suspending agents such as PVP (col. 18, line 43 to col.19, line 5). Agents such as tartaric acid (solubilizers), mannitol (fluidizers), sucrose, and sodium chloride are taught. The reference teaches a semipermeable wall that allows water to enter the core. A semipermeable wall made of 95% cellulose acetate having an acetyl content of 39.8% and 5% PEG surrounds the two compositions. The coating has pore sizes of 10 angstorm to 100 microns See column 10 to column 11, line 20. . Solvents for the semipermeable membrane are taught on column 20, lines 11-35. Release of the drug is taught in Figure 9. Wong teaches several shapes such as in Figure 5, wherein rather than have one port as seen in a tablet, the device as several pores to allow the passage of water. Wong teaches that the shape of the tablet and capsule shape are different, they act in a similar manner to let fluid into the core. See column 8. Solvents for the

semipermeable membrane are taught on column 20, lines 11-35. Release of the drug is taught in Figure 9.

Wong does not teach instant parameters and swelling agents.

Stevens et al teach a delivery device with a drug and expandable excipient. The dosage form may be in tablet form. See abstract and examples. The device has an impermeable coating formed from a water soluble material. See column 3, lines 13-21. The expandable excipient is also a water-swellable material that has the overall swelling capacity of 200-400% (col. 4, lines 44-48). The swellable materials may be chosen from PEO polymers, sodium starch glycolate, microcrystalline cellulose, etc. (col.3-4). The expandable excipients also contain wetting agents (sodium lauryl sulfate) up to 2%, lubricants such as magnesium stearate and silica up to 1%, and water soluble sugars up to 10%. Stevens teaches the conventional hardness of a tablet is 4kg (col. 5, lines 5-70. The drug may be mixed with a carrier material and is positioned over the hydrogel layer (col. 6, lines 26-27). The swelling factor is taught on column 7. The device has the advantage of containing expandable excipients that are designed to improve the expulsion of the active in a particular region such as the gastric tract that has low water content. See column 5.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Wong et al and Steven et al and utilize the instant swelling agent. One would be motivated to utilize the instant swelling agent in the expandable hydrogel portion since Stevens et al discloses that the instant swelling capacity improves the release of an active in the gastro-intestinal tract.

Therefore one would be motivated to utilize the instant swelling agent to yield the instant swelling ratio and provide improved target delivery. Further, one would expect similar results since Wong's expandable portion contains PEO and Stevens teaches substituting the PEO hydrogel powder with swelling agent to enhance to rate of deliver since the swelling agent rapidly absorbs water or optionally mixing of swelling agents as seen in the examples

Response to Arguments

Applicant argues that as shown in the Rule 132 declaration, Wong et a do not teach the instant swelling ratio. Applicant argues that there is no discussion regarding using higher swellable material or the difficulty of compressing tablets or the use of tabletting aids in the water-swellable portion. Applicant argues that Stevens does not disclose an osmotic tablet and that Stevens teaches a capsule. It is argued that Stevens does not recognize the need to achieve good tablet strength. Applicant argues that although Stevens teaches minor adjuvants for the expandable excipients, the reference does not recognize the need to use these adjuvants to improve tabletting.

First it is pointed out that the Rule 132 declaration served to demonstrate that US patent 5,620,705 did not have the instant swelling ratio. The Rule 132 does not apply to US 4,765,989 and instant rejection. Second, the examiner already has recognized the deficiency in Wong et al as set forth in the rejection. Wong does not teach the instant swelling material that yields the instant swelling ratio. Therefore a secondary reference is relied upon for this teaching. It is the examiner's position that Steven's swelling material may be substituted into water swellable potion. One would be motivated to do

since instant swelling capacity allows for an improved release of the agent and Stevens teaches that certain PEO's and the instant swelling agents provide the instant swelling capacity. Thus, since Wong teaches PEO in the water-swellable portion, there is an expectation of similar results.

In regards to the tabletting aid, the examiner points to the examples wherein the water-swellable composition does include a tabletting aid (magnesium stearate). Further, it is pointed out that the use of reference are not limited to what the patentee describes as in invention or the problems which they are trying to solve, they are part of the literature of the art, for all they contain. Therefore, Wong does not have to discuss the applicant's problem and the applicant's reason for combining need not be that of the examiner's. In regards to Stevens and as recognized by the applicant, Stevens does not teach the instant tabletting aids in the water-swellable composition. Note the examples. Thus, the fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985). Thus, even though neither reference discusses the reason to use a tabletting aid, the references use it nonetheless and applicant's result will naturally be yielded.

In regards to the argument that Stevens only teaches capsules, the examiner points out that the secondary reference is solely relied upon for the swelling material and the swelling capacity; Wong encompasses the broad aspect of the invention. Further, it is pointed out that Stevens clearly teaches that the expandable excipients

may be in tablet form. Additionally, both reference function similarly. Both references contain hydrogels that expand to release the active. Therefore, both Stevens and Wong are in the same field of endeavor and are directed to the same goal of controlled release. Lastly, although the applicant argues that the instant invention is directed towards tablets, it is pointed out that the claims are only limited to a generic dosage form.

In regards to the argument that the examiner has not addressed some of the limitations, the examiner points out that all limitations have been addressed. Firstly, the applicant defines solubilizers as acids, surfactants, etc on page 22 of instant specification. Clearly, Wong teaches wetting agents (surfactants) and acids (tartaric acid) in the drug composition. Note column 14, line 62 to column 15, line 15. Applicant argues that Wong teaches these as osmotic solutes and not solubilizers. The use of a different term than the prior art; i.e. solubilizer versus osmotic solutes, does not hold patentable weight since the claims are directed towards product claims. Further, the ingredient will act the same in the composition. This holds true for applicant's argument regarding the lack of teaching of the fluidizing agent. On page 21 of the instant specification, the applicant defines the fluidizing agent as sugars such as lactose, mannitol, sucrose, etc. Wong clearly teaches these sugars in Table 1. Applicant argues that Wong does not teach that the fluidizing agent is selected based on its ability to be high soluble and should be used in a minimum amount to be effective. The examiner points out that the claims are directed to a product and the role of an individual ingredient does not have patentable weight. In regards to the weight argument, the

examiner points out that the claims do not recite a weight percentage of the fluidizing agent and applicant's arguments rely on a feature that is not in the claims. The examiner points out that Wong does teach concentrating polymers. The applicant defines concentrating polymers as PVP and cellulose derivatives on page 25 of instant specification and dependent claims. The examiner points to the drug composition in example 3 of Wong, which contains HPMC. The examiner points to column 19 wherein Wong clearly teaches that the drug can be combined with PVP which meets the claim of 119 wherein the drug is dispersed in a concentrating enhancing polymer. Further, it is pointed out that Wong teaches that the drug can take many forms such as a suspension or a soluble form. A suspension is defined as "the state of a substance when its particles are mixed with but undissolved in a fluid."

Lastly in regards to the argument to the tablet strength, Stevens clearly teaches it is conventional for tablets to have the instant hardness and therefore in the absence of unexpected results, it is the examiner's position that this is a manipulative parameter in the art. Further, Stevens states that the tablet does not have to have the strength of conventional tablets but does not state that the tablets cannot or does not have the instant strength.

Claim 57 is rejected under 35 U.S.C. 103(a) as being unpatentable over Wong et al (4,765,989) in view of Stevens et al (5,897,874) in further view of From hypertension to angina to Viagra (Jim Kling, Modern Drug Discovery, 1998, 1(2), 31, 33-34, 36, 38.)

As set forth above, Wong and Stevens teach delivery devices containing expandable excipients. Wong teaches the suitability of several drugs such as antihypertensives.

Wong and Stevens do not teach instant drug

Kling teaches Viagra as a drug for hypertension or erectile dysfunction.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use sildenafil citrate in the device of Wong or Stevens. One would be motivated to do so if one wanted to treat erectile dysfunction and it is obvious for an artisan to choose the drug depending on the symptoms and disease to be treated. Further, one would be motivated to do so with the expectation of similar results since Wong teaches the use of antihypertensives in the device.

Claims 2, 7-9, 12-32, 44-45, 49-56, 63-81, 88-97, 101, 103-108, 118-122, 124, and 130-131 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wong et al (4,765,989) in view of Park et al (6,271,278).

Wong et al teach an osmotic device for administering drugs in various shapes and forms. The object of the device is to provide a therapeutic device that administers a complete pharmaceutical regimen at a controlled and continuous time period. The device also provides dispending to the gastric tract at a controlled rate. See column 3. The device contains a first composition containing a drug, polyethyleneoxide (PEO) (drug entertaining agent), hydroxypropylmethylcellulose (HPMC) (concentration enhancing polymer), and magnesium stearate (tabletting aid). The second expanding composition contains PEO (swelling agent), HPMC (concentration enhancing polymer),

sodium chloride, and magnesium stearate (tabletting aid). The osmopolymers used in the invention have an expansion factor of 2-50 fold volume increase in the presence of aqueous or biological fluid (col. 16, lines 3-5). The mass ratio of the first composition to the second composition is taught on column 16. The swelling ratio is taught on columns 17 and 18. Wong teaches the active agent may in various forms and dispersed in suspending agents such as PVP (col. 18, line 43 to col.19, line 5). Agents such as tartaric acid (solubilizers), mannitol (fluidizers), sucrose, and sodium chloride are taught. The reference teaches a semipermeable wall that allows water to enter the core. A semipermeable wall made of 95% cellulose acetate having an acetyl content of 39.8% and 5% PEG surrounds the two compositions. The coating has pore sizes of 10 angstorm to 100 microns See column 10 to column 11, line 20. . Solvents for the semipermeable membrane are taught on column 20, lines 11-35. Release of the drug is taught in Figure 9. Wong teaches several shapes such as in Figure 5, wherein rather than have one port as seen in a tablet, the device as several pores to allow the passage of water. Wong teaches that the shape of the tablet and capsule shape are different, they act in a similar manner to let fluid into the core. See column 8. Solvents for the semipermeable membrane are taught on column 20, lines 11-35. Release of the drug is taught in Figure 9.

Wong does not teach instant parameters and instant swelling agent.

Park et al teach a hydrogel composition having fast swelling and high mechanical strength. The superporous hydrogel composite is formed by polymerizing one or more ethylenically-unsaturated monomers, and a crosslinking agent, in the presence of

particles of a disintegrant. The disintegrant such as crosslinked sodium carboxymethylcellulose, crosslinked sodium starch glycolate, and crosslinked PVP, rapidly absorbs water and serves to increase mechanical strength. See abstract. Park discloses that the limiting factor of hydrogels have been their slow swelling property which usually takes several hours and this it too slow for many applications when fast swelling is essential. Park discloses that although hydrogels have been successfully used as gastric retention devices that stay in the stomach for several hours, the hydrogels had to be preswollen before administering to avoid premature emptying into the intestine. Further, Park discloses to increase g properties, the mechanical strength decreases; however by adding the disintegrant, the mechanical strength is increased. See column 4, lines 10-45 and column 26. The ratio of polymer to disintegrant is taught to be 1:1000 to 100:100. See column 7, line 8. Swelling ratios are taught on Table 2. Compression is taught in Figure 4A in kg/cm2. Park teaches that in the controlled drug delivery area superporous hydrogel and superporous hydrogel composites can be used as a platform for long-term oral drug delivery. For to the fast swelling and superswelling properties, they can stay in the stomach for a few hours to more than 24 hours. Thus, such long-term gastric retention is ideal for long term controlled drug delivery.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Wong et al and Park et al and instant swelling capacity (ratio) and swelling agents. One would be motivated to do so since Park discloses that a fast swelling hydrogel and superswellling is important for controlled oral dosage forms. Further, motivation to do so being that Park discloses that

the superabsorbent hydrogel is an improvement over the prior art's hydrogels since it not only possess super swelling capacity but is also has increased mechanical strength by using instant swelling agents. Therefore, one would be motivated to add Park's hydrogel into Wong's second composition for the stated advantages. Further one would expect similar results, since Park states the hydrogel may be used as a platform in controlled dosage forms. Therefore, Parks' hydrogel would fit directly into Wong's second expandable composition since both are designed for the same purpose of swelling in contact with biological fluids and thus releasing the active.

Claim 57 is rejected under 35 U.S.C. 103(a) as being unpatentable over Wong et al (4,765,989) in view of in Park et al (6,271,278) further view of From hypertension to angina to Viagra (Jim Kling, Modern Drug Discovery, 1998, 1(2), 31, 33-34, 36, 38.)

As set forth above, Wong and Park teach delivery devices containing expandable excipients. Wong teaches the suitability of several drugs such as antihypertensives.

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Kling teaches Viagra as a drug for hypertension or erectile dysfunction.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use sildenafil citrate in the device of Wong. One would be motivated to do so if one wanted to treat erectile dysfunction and it is obvious for an artisan to choose the drug depending on the symptoms and disease to be treated. Further, one would be motivated to do so with the expectation of similar results since Wong teaches the use of antihypertensives in the device.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharmila S. Gollamudi whose telephone number is (703) 305-2147. The examiner can normally be reached on M-F (7:30-4:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman Page can be reached on (703) 308-2927. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

SSG
10/24/03

MICHAEL G. HARTLEY
PRIMARY EXAMINER